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Oral Lichen Planus: An Update on Etiology, Pathogenesis and Management - A Review of Literature

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ABSTRACT

Background: Lichen planus is a chronic inflammatory mucocutaneous disease. Mucosal lesions are classified into six clinical forms and there is malignant potential for Oral Lichen Planus (OLP); therefore, follow-up should be considered. There are many unestablished etiological factors for OLP. A genetic predisposition linked to Th1 cytokine polymorphisms may promote the T cell-mediated immunological response to an induced antigenic change that is supposed to lead to OLP lesions. Some putative etiologic factors, mainly amalgam restorations and hepatitis C virus have been studied in detail. The diagnosis of OLP can be made from the clinical features if they are sufficiently characteristic, but biopsy is recommended to confirm the diagnosis, exclude dysplasia and malignancy and if active treatment is required. The aims of current OLP therapy are to eliminate mucosal erythema and ulceration, alleviate symptoms and reduce the risk of oral cancer. The management of OLP is mainly aimed at controlling the symptoms and topical immunomodulators such as powerful corticosteroids and calcineurin inhibitors have been used. However their long-term effects needs to be better explained and understood.

Keywords: Dental Restoration, Retroplast, Geristore, Mineral Trioxide Aggregate.

INTRODUCTION

The term Lichen Planus was initially introduced by Erasmus Wilson in 1869 to describe the condition that had been previously named leichen ruber by Hebra. The term lichen is derived from greek word “leichen” which means “treemoss”. The word Planus comes from Latin which means “smooth, level or even”. Lichen planus is a chronic inflammatory mucocutaneous disease which frequently involves the oral mucosa. In the majority of patients with oral lichen planus (OLP), there is no associated cutaneous lichen planus or lichen planus at other mucosal sites. This may be called “isolated” OLP[1]. This disease has most often been reported in middle-aged patients 30 - 60 years of age and is more common in females than in males.[2] OLP is also seen in children, although it is rare[3].

The prevalence of lichen planus is unknown, but it is estimated to occur in <1% of the population. It is thought to be significantly less frequent than exclusive OLP that affects approximately 1-2% of the population. Estimates of prevalence vary among different populations, but the condition does not appear to exhibit a racial predilection. Whereas in the majority of instances cutaneous lesions of lichen planus (LP) are self-limiting and cause itching; lesions in OLP are chronic, rarely undergo spontaneous remission, are

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potentially premalignant and are frequently a source of morbidity[4].

ETIOLOGY

Virtually all diseases result from the interplay of host, lifestyle and environmental factors, including oral lichen planus. Although the etiology has not been fully elucidated, an immunologically induced degeneration of the basal cell layer of the oral mucosa has been suggested. In the past, speculation about the etiology covered a wide range of possibilities including trauma, specific bacteria, syphilis, parasites, viruses, mycotics, allergies, toxicity, neurogenic, hereditary, and psychosomatic disorders[5].

Autoimmunity

Auto immunity has been suggested as a basis for the lesions of lichen planus. Autoimmune disorders classically have a marked female predisposition, are associated with serum auto antibodies (which may be detectable in the tissues) with a hypergammaglobulinaemia, and with other autoimmune disorders, but, auto antibodies only are uncommonly detected in lichen planus and antinuclear antibodies are detected in low titer and in a minority while anti-DNA antibodies are not found[5].

Immuno-deficiency

Serum immunoglobulins :

Sklavounou AD et al (1983) in their study found significantly increased levels of serum IgG ($p < 0.05$) and a significant reduction of serum IgA concentration ($p < 0.05$) in the oral lichen planus cases as compared with normal controls. These results suggest that patients with oral lichen planus may have a generalized immunologic disorder in which humoral immunity is disturbed[6].

Cell-mediated immunity

Scully et al (1998) reported that cutaneous LP is more strongly associated with defects of T-cell function like thymoma and stated that there is no consistent alteration in the serum levels of immunoglobulins in OLP[7].

Genetic factors in lichen planus

Familial occurrence of LP is a well-recognized but rare event, with an incidence varying from 1% to 11% of all LP patients. In comparison with classic LP, familial LP is characterized by its early age of onset, atypical and widespread clinical presentation, and its higher tendency to become severe and chronic[8].

Psychogenic factors

Emotional Stress was implicated as an important etiological factor in oral lichen planus. It is observed that certain intense and prolonged emotional stresses such as anxiety, shock, traumatic childhood, sadness; disappointment, failure, humiliation often initiate the process of Lichen Planus. Stress is also identified as most important cause of exacerbation of OLP.

Altman and Perry[9] reported in a study of 197 patients with LP that only 10% of patients recall stressful situation at most of the disease whereas 60% patient believes chronic stress aggravated its course.

Habits and oral hygiene

Gorsky M et al (2004) showed that fewer cases of reticular OLP were symptomatic than erosive OLP. Significantly fewer OLP patients smoked than the control group. More patients with reticular OLP smoked than those with atrophic and erosive OLP. It is hypothesized that the heat and irritation of smoking may aggravate symptomatic OLP lesions, and the risk of malignant transformation associated with tobacco use may play a role in patients stopping tobacco use[10].

Drugs and chemicals

Certain modern medicines such as non-steroidal anti-inflammatory pain killers (NSAID), antihypertensive medicines, amalgamated dental filling, etc. are known to induce Lichen Planus, which has a tendency to persist despite the discontinuation of the said medicines.

Medicines which are known to induce Lichen Planus are:

NSAIDs (Non-steroidal anti-inflammatory drugs), Tetracycline, Captopril, Propranolol, Sulfonamide, Dapsone, Furosemide, Chloroquine,

Penicillamine, Methyldopa, Enalapril and Allopurinol (anti-gout medicine).

Systemic diseases

Lodi G *et al*. reported that lichen planus is sometimes associated with infections or auto immune diseases and/or neoplasia, but the association had not been established. Certain systemic diseases like diabetes mellitus, hypertension, ulcerative colitis, myasthenia gravis, lupus erythematosus etc. were considered to be associated with OLP. A more consistent association was found between chronic liver disease and erosive form of OLP[11].

Infective agents

Herpes, Human papilloma virus, Hepatitis C virus infection[12] are certain infective agents known to cause OLP.

Pathophysiology

The cause of LP is not known but immunologic mechanisms triggered by poorly defined antigenic stimulations play a pivotal role in the pathogenesis of the disease. Cell-mediated immune response is believed to play the major role in the pathology of the disease. Presence of activated antigen presenting cells (Langerhans' cells, dendritic macrophages) in the lesional skin could be demonstrated in the early stage of the disease. CD4+ cells initiates immune response in which activated keratinocytes also take part. CD8+ T lymphocytes mediate the damage to the epidermis and leads to the characteristic lichenoid tissue reaction. Lichen Planus is found to be an immunologically mediated disease. Some triggers have been found which are clinically found to be responsible for Lichen Planus.

Current data suggest that oral lichen planus is a T-cell–mediated autoimmune disease in which autocytotoxic CD8+ T cells trigger apoptosis of oral epithelial cells.

The dense sub-epithelial mononuclear infiltrate in oral lichen planus is composed of T cells and macrophages, and there are increased numbers of intra-epithelial T cells. Most T cells in the epithelium and adjacent to the damaged basal keratinocytes are activated CD8+ lymphocytes. Therefore, early in the formation of oral lichen planus lesions, CD8+ T cells may recognize an antigen associated with the major histocompatibility complex (MHC) class I on keratinocytes. After antigen recognition and activation, CD8+ cytotoxic T cells may trigger keratinocyte apoptosis. Activated CD8+ T cells (and possibly keratinocytes) may release cytokines that attract additional lymphocytes into the developing lesion[13].

CLINICAL FEATURES

General

Oral lichen planus affects 1-2 per cent of the general adult population. Is planus occurs predominantly in adults over 40, although younger adults and children may be affected. It occurs in adulthood with atleast two-third of the cases occurring between 30-60 years and is observed in nervous 'highly strung" people' The prevalence of LP in general population is about 0.9-1.3 % and prevalence of oral lichen planus is reported between 0.1-2.2%[14]. Shklar (1972) stated that in routine dental clinic the prevalence is about 0.6% and Moshella SL et al have stated the incidence to vary between 0.1% and 0.2%[15].

Females are affected between the ages of 45-54 years while males are affected between 35-44 years. It has seen to have predilection for females, with a female to male ratio of 1.4:1, although some authors believe that there exists no sex predilection.[16] Other authors like Andreason J.O (1968), Laufer (1971), Lacy M.F et al (1983), Regezi J.A (1989), Rose L.F (1990) have also reported female predilection in lichen planus[17,18]. Neville B.W. et al (1995) have reported a ratio of 3:2 for women to men while Chiapelli F. et al (1997) noted that women were 1.5 to 2.0 times at greater risk than men[19,20].

The six P's of lichen planus that characterize the lesions are planar, polygonal, purple, pruritic, papules and plaques. The lesions often occur bilaterally, intraorally and on the flexor surfaces of the extremities. The clinical spectrum of lichen planus is broad and may involve skin, mucous membrane, nails and hair[17].

The symptoms in cutaneous lichen planus include intense pruritis with signs of a

characteristic violet hue and flat topped shiny, polygonal papules and plaques, the surface of which is usually dry and thin with adherent scales; while OLP is mostly asymptomatic except when associated with chronic atrophic/ulcerative erosive lesions which commonly give rise to pain[17].

Lesions are typically bilateral and often appear as a mixture of clinical subtypes. White or grey streaks may form a linear or reticular pattern on an erythematous background. Oral lichen planus presents as white striations, white papules, white plaques, erythema, erosions or blisters affecting predominantly the buccal mucosa, tongue and gingivae, although other sites are occasionally involved[14].

Oral Lichen Planus - Types

Andreasen (1968)[17] divided oral lichen planus into six types: reticular, papular, plaque-like, erosive, atrophic, and bullous. The reticular, papular, and plaque-like forms are usually painless and appear clinically as white keratotic lesions. The erosive, atrophic, and bullous forms are often associated with a burning sensation and in many cases can cause severe pain.

Mucosal lesions, which are multiple, generally have a symmetrical distribution, particularly on the mucosa of the cheeks, adjacent to molars, and on the mucosa of the tongue, less frequently on the mucosa of the lips (lichenous cheilitis) and on the gums (the atrophic and erosive forms localized on the gums manifest as a desquamative gingivitis), more rarely on the palate and floor of the mouth. However, this clinical appearance of desquamative gingivitis is not pathognomonic of erosive OLP and may represent the gingival manifestation of many other diseases such as cicatrical phemphigoid, pemphigus vulgaris, epidermolysis bullosa acquisita, and linear IgA disease. The most common type is reticular form with the characteristic feature of slender white lines (Wickham's striae) radiating from the papules. Patients with reticular lesions are often asymptomatic, but atrophic (erythematous) or erosive (ulcerative) OLP is often associated with a burning sensation and pain. A greater malignant potential has been recognized for atrophic, erosive form of OLP and the plaques form on the back of the tongue. Mignogna et al have suggested that regular follow-up of patients with OLP should be performed up to 3 times a year. OLP with dysplasia should be examined more frequently, every 2-3 months. However, patients with asymptomatic, mainly reticular type may be assessed annually. The signs that may be indicative of transformation, such as the extent of symptoms and loss of homogeneity, should be assessed thoroughly at each appointment. When there is evidence of changes in clinical appearance, the follow-up period should be shortened and biopsy should be provided[21].

Management of OLP

The main aim of any therapy of OLP is symptomatic control. Usually, patients with reticular and other asymptomatic OLP lesions do not require active treatment. Precipitating factors and irritants such as maloccluded or fractured teeth, poorly fitting dentures, alcohol and tobacco consumption should be identified and avoided or eliminated wherever possible[4].

Several treatment regimens have been proposed to improve management of symptomatic oral LP, but a permanent cure is not yet available. Notably, several suggested treatment modalities are also suspected to induce lichenoid lesions. Topical treatment is generally preferred as it has fewer adverse effects. However, systemic agents may be required if lesions are widespread and mainly involve the skin or other mucosae, or the disease is recalcitrant to topical medications. Drugs for OLP are fundamentally immunosuppressive and were not generally developed for oral diseases. As a result, there is a lack of adequate studies determining their efficacy and optimal dose, duration of treatment and safety remain largely unknown[4].

Topical corticosteroids

A positive response to treatment with midpotency corticosteroids such as triamcinolone acetonide 0.1%, potent fluorinated corticosteroids such as fluocinolone acetonide 0.1%, fluocinonide 0.05% and super potent halogenated corticosteroids such as clobetasol propionate 0.05% has been reported in the majority of treated patients. Particularly, clobetasol propionate appears to be the most effective topical steroid with 56% to

75% of the patients undergoing a complete remission of signs and symptoms[22].

Pseudo membranous candidiasis is the only common side effect from topical corticosteroid therapy. This can be prevented with antifungal use (such as miconazole gel) alone or with chlorhexidine mouthwashes[4].

Other topical agents

Other immunomodulatory agents such as calcineurin inhibitors (cyclosporin, tacrolimus, or pimecrolimus) or retinoids can be beneficial mainly if the lesions are recalcitrant to the most powerful steroids. Cyclosporin has been used as a mouth rinse (50-1500 mg/day) or in adhesive bases (26-48 mg/day) but is expensive, not always effective and less effective than topical clobetasol in inducing clinical improvement in OLP, though the two drugs do have comparable effects on symptoms. Tacrolimus is 10-100 times as potent as cyclosporin and has greater percutaneous absorption than cyclosporin. Pimecrolimus is the newest calcineurin inhibitor used in OLP treatment. Its action is similar to that of tacrolimus but has no effect on Langerhans cells. The immunosuppressant capacity of pimecrolimus is weaker than cyclosporin or tacrolimus and it has lower permeation through the skin than topical steroids or topical tacrolimus[4].

Systemic drug treatment

Systemic corticosteroids are usually reserved for cases where topical approaches have failed or for widespread OLP when skin, genitals, oesophagus, or scalp are also involved. Prednisolone 40 to 80 mg daily is usually sufficient to achieve a response when taken either for brief periods of time, (5-7 days) and then withdrawn abruptly, or the dose is reduced by 5–10 mg/day gradually over 2-4 weeks[4]. Very recently, also biologic agents including Basiliximab, Etanercept, Efalizumab and Alefacept have been proposed for OLP treatment[23,24].

Surgical treatment

Non-pharmacological modalities such as phototherapy, surgery and laser treatment (with both carbon dioxide and low dose excimer 308-nm laser) have been suggested mainly in patients recalcitrant to more conventional modalities but their effectiveness is yet to be proven and surgical intervention has also been reported to provoke OLP[4].

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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